AWARD NUMBER: DAMD17-97-1-7144

TITLE: Tomosynthesis Breast Imaging:
Early Detection and Characterization of Breast Cancer

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REPORT DATE: July 1999

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Material Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	July 1999	Annual (1 Jul 98 - 30 Jun 99)

4. TITLE AND SUBTITLE
Tomosynthesis Breast Imaging: Early Detection and Characterization of Breast Cancer

5. FUNDING NUMBERS
DAMD17-97-1-7144

6. AUTHOR(S)
Leena M. Hamberg, Ph.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Massachusetts General Hospital
Boston, Massachusetts 02114

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Matereiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 Words)*

14. SUBJECT TERMS
Breast Cancer

15. NUMBER OF PAGES
14

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

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L. Hamberg

PI - Signature Date

ANNUAL REPORT

TOMOSYNTHESIS BREAST IMAGING: EARLY DETECTION AND CHARACTERIZATION OF BREAST CANCER

Contents

ANNUAL REPORT

TOMOSYNTHESIS BREAST IMAGING: EARLY DETECTION AND CHARACTERIZATION OF BREAST CANCER (DAMD-97-1-7144)

Our aim for the second year of this grant was to investigate the tomosynthetic image quality by performing experimental studies using the specially developed phantoms and to quantitate tomosynthesis image quality parameters by using image post processing. Moreover we have further improved the tomosynthetic image reconstruction by implementing faster and more versatile image reconstruction algorithm. In addition, we have investigated the low contrast lesion detection characteristics of our digital mammography system capable of tomosynthesis and did a comparison with a conventional film/screen technique.

A. INTRODUCTION

Advances in computer technology and the introduction of new digital imaging detectors offer not only the potential for digital image acquisition but also for development of new mammographic imaging techniques. Digital tomosynthesis of a breast is a mammographic imaging technique whereby to obtain tomosynthetic images a set of digital images is acquired as the X-ray source is moved in an arc above the breast. Any plane of the breast can be brought into a sharp focus while structures outside the selected focal plane are blurred [Niklason et. al., Radiology 1997; 205:399-406]. Tomosynthesis mammography may become an important tool for breast cancer screening and lesion characterization as it potentially offers a better visualization of a lesion by blurring radiographically dense fibroglandular breast tissue overlying the cancer.

We have implemented a tomosynthesis technique on a full-field digital mammography unit, which has high detective quantum efficiency (higher than film screen systems), low noise and large detector area with rapid readout times (300 msec). The detector is composed of a Cesium Iodide (CsI) phosphor in direct contact with an amorphous silicon photodiode/transistor array. The columnar structure of CsI phosphor directs the light produced in each x-ray interaction with the scintillator toward the silicon detector with very little lateral diffusion yielding a high spatial resolution. The spatial resolution measured by the modulation transfer function (MTF) out to the Nyquist frequency (5 lp/mm for 100um pixel pitch) is similar to that of the highest resolution presently achievable with mammography films.

The tomosynthesis images are digitally reconstructed from a number of 2-dimensional projection images acquired by moving an X-ray tube in an arc above the object. Thus a final tomosynthesis image is a calculated image reconstructed from many projection images and the quality of a tomosynthetic image may differ from a single digital mammogram and may vary as a function of several imaging parameters such as x-ray tube voltage, x-ray tube current, target-filter combination, the extent of the x-ray tube arc, number of projections acquired, and the photon fluence per projection.

Our aims were to determine experimentally the tomosynthetic image quality by acquiring image data using the specially developed tomosynthesis phantoms (wire phantom and a complex background phantom) and by analyzing the data through quantitative image post-processing techniques.

B. METHODS

B.1. RECONSTRCUTION ALGORITHM

Our earlier algorithms for tomosynthesis image reconstruction are MATLAB applications and can be used only on a system that has MATLAB running on that system. Recently we implemented a backprojection algorithm for tomosynthesis image reconstructions using C++-programming language. This has made the reconstruction process not only much faster but also more flexible. Our new algorithm allows partial image reconstructions using varying regions of interest within the field of view or within the detector area. Moreover the gridsize, i.e. the output image matrix size, is implemented as an input parameter making reconstructions with varying matrices possible.

B.2. TOMOSYNTHESIS IMAGE QUALITY

To characterize the tomosynthesis image quality we designed and manufactured a "wire" phantom. This phantom includes two angled wires (7° and 60°) for the determination of the modulation transfer function (MTF) for the system. From the MTF the spatial resolution in a tomosynthetic image can be obtained. In addition, the wire phantom can be used for estimating the tomosynthetic slice thickness, which changes as a function of the extent of the arc the projection images are acquired. An alternate, visual manner for the spatial resolution determination is provided by a line pair pattern embedded at 25mm depth of the 230mm*180mm*50mm (Length*Width*Height) block of BR12 material.

B.2.1. Spatial Resolution of a Tomosynthetic Mammographic Image

We studied the spatial resolution in a tomosynthetic image as a function of views, rotation angle used for the data acquisition and as a function of dose. We imaged the

wire phantom using various combinations of projections and rotation angles and mAs/projection. From the reconstructed images we determined the line spread functions (LSF) and took a Fourier Transformation of the LSF yielding the modulation transfer function (MTF) for a tomosynthetic image. Figures 1 and 2 are presentations of the MTF as a function of projections and as a function of the total rotation angle.

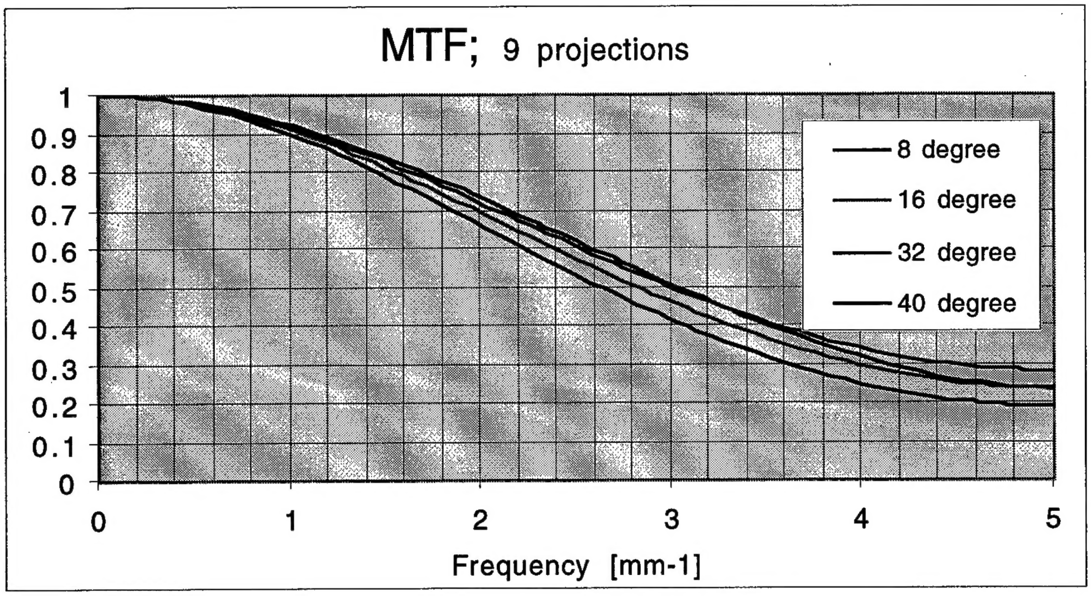

Figure 1. The graphs represent the modulation transfer functions obtained using 9 views but varying the arc of the tube rotation; i.e. the total angle. The cut-off frequency does not change significantly as a function of the angle and is about the same as measured in 2-dimensional, projection, and digital mammograms.

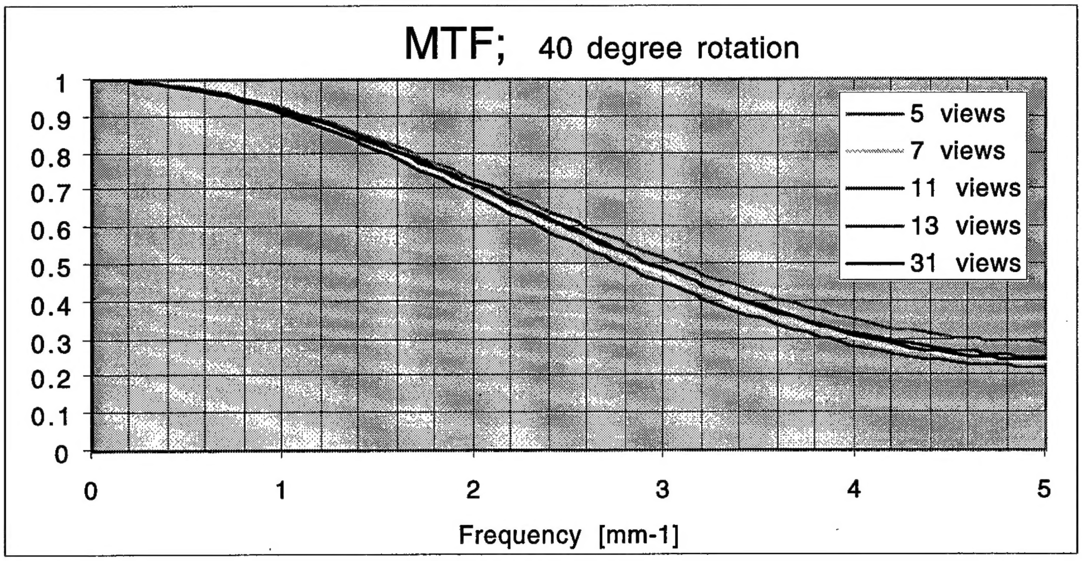

Figure 2. The graphs represent the modulation transfer functions (MTF) obtained using a 40 degree rotation angle and varying number of views. The cut-off frequency does not change significantly as the number of the projections changes.

B.2.2. Signal-to-Noise Ratio (SNR) in a Tomosynthetic Mammographic Image

We characterized the SNR ratio in tomosynthesis images at an equivalent radiation dose to the one used to obtain a normal mammogram as well as at higher doses of 1.3, 1.5 and 2 times the dose of a normal mammogram. The number of projection views and the angle of the rotation arc were kept constant for these measurements.

B.2.3. Tomographic Slice Thickness

We measured the in-focus, tomographic, slice thickness using the developed wire phantom. As tomographic angle increases the slice thickness decreases. The angles used ranged from 8° to 40° and the corresponding slice thicknesses changed from 2.8mm to 0.9mm.

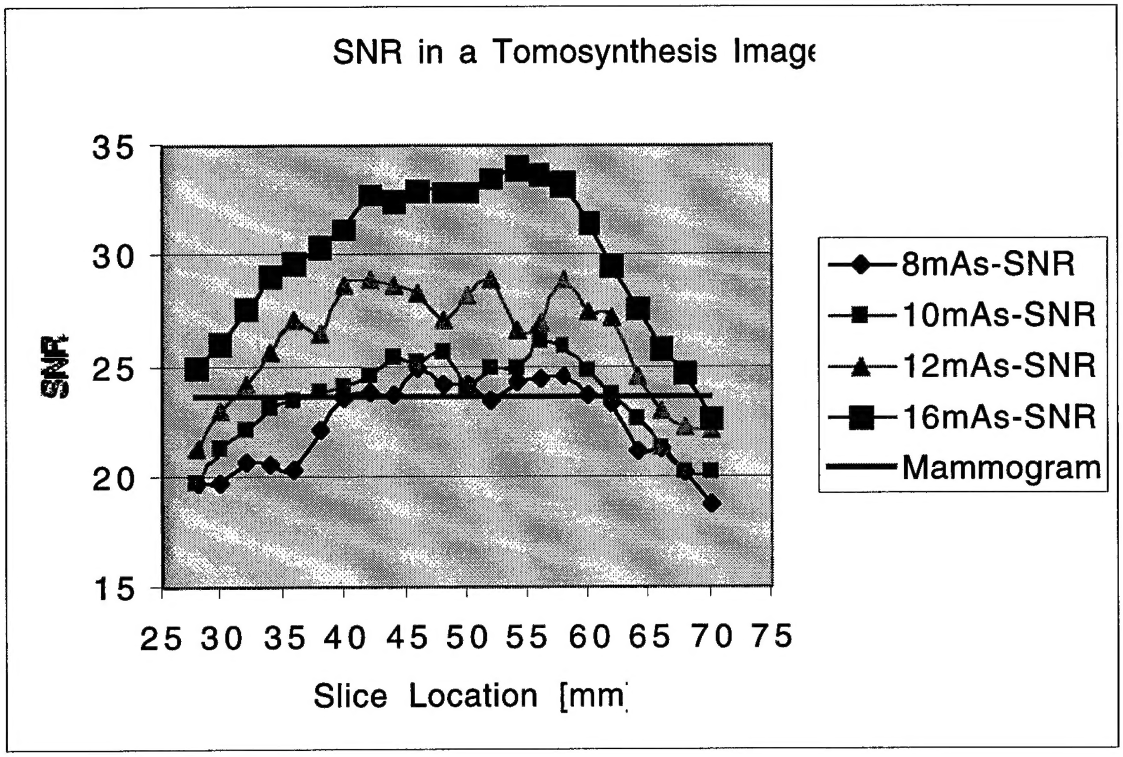

Figure 3. A presentation of the signal to noise ratio (SNR) for a 300 micron thick calcification. The SNR was measured as a function of the slice location and as a function of the entrance dose. It can be seen that SNR is highest around the focal plane (515mm) and decreases as the slice location moves away from the focal plane. In addition, the SNR increases with increasing dose. However, even the lowest dose SNR in a tomosynthesis image is slightly higher than in a conventional mammogram obtained using an equivalent dose.

B.3. LESION DETECTION WITH DIGITAL TOMOSYNTHESIS

We compared the low contrast lesion detection in full-field digital mammography images and conventional film-screen images using a contrast-detail phantom containing gold disks of thicknesses from 0.05 to 1.6 microns and 0.1 to 3.2 mm in diameter. Both images, digital and film-screen, were obtained using equivalent technique factors. On the digital system we assessed image lesion detection capability as a function of dose and target/filter type and acquired the images at both 50μm and 100μm pixel size. The digital images had a significantly lower ($p<0.05$) object contrast threshold (allowed detection of thinner objects) than screen-film images for all studied techniques and target/filter combinations. Moreover, the lesion-detection using the digital system was superior to conventional screen-film system even using half of the radiation dose of that was used to acquire a conventional screen-film image.

In tomosynthetic images, we also found that the lesion detection was better than in 2-dimensional, digital mammograms. We used our complex phantom as an object where the signal plate was sandwiched in the middle of the complex background plates. In Figure 4 a 2-dimensional digital mammogram and a tomosynthetic image of the complex phantom is shown. On a 2-dimensional image, it is difficult to see any of the spiculated, lobulated or round masses, however, in the tomosynthesis image three spiculated, three lobulated and three round masses are easily seen. In addition, two clusters of calcifications are seen on a tomosynthesis image while none of them are visible on the 2-dimensional mammogram.

(A)

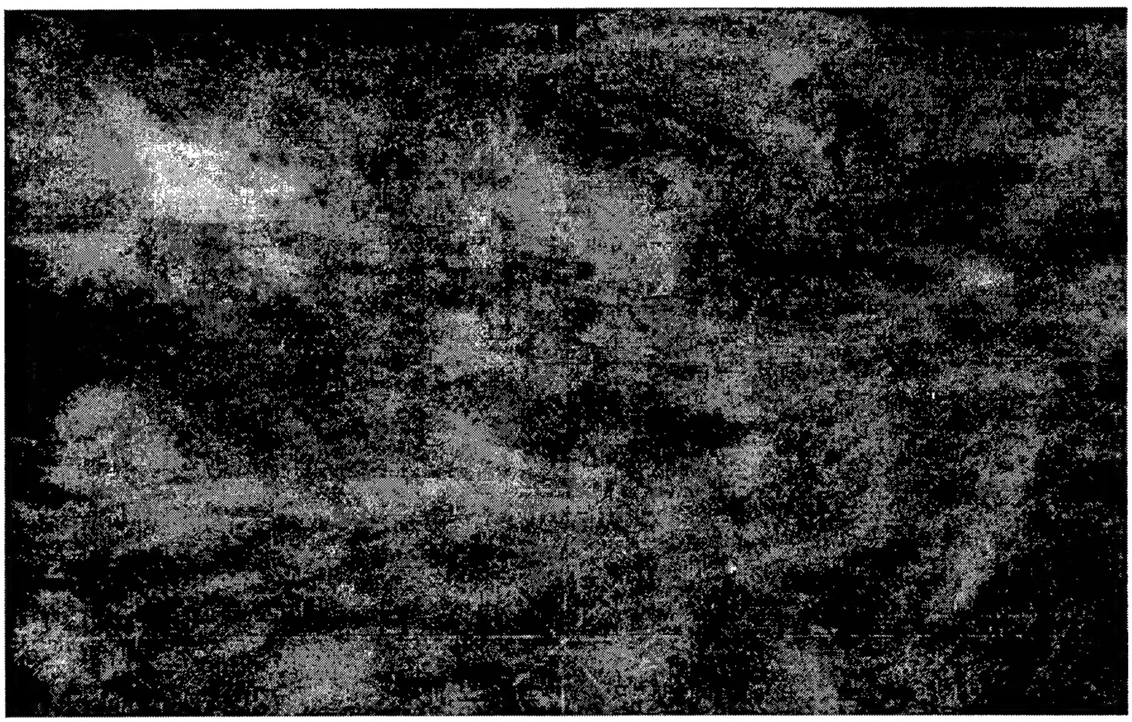

Figure 4. **(A)** A 2-dimensional mammogram of the complex phantom. Only 1 spiculated, one lobular and one round lesion can be seen. **(B)** In a tomosynthetic image 3 spiculated, 3 lobulated and 3 round masses are visible as well as 2 calcification clusters.

(B)

B.4. PHANTOM DEVELOPMENT

B.4.1. Wire Phantom

The "wire phantom" was designed for studies of measuring spatial resolution in tomosynthesis images. It includes two wires, one deep and one shallow wire that travel 7° and 60° to the vertical direction. The wire can be used for the determination of the modulation transfer function (MTF) and spatial resolution for the tomosynthesis system. In addition the tomosynthetic slice thickness, which changes as a function of the extent of the arc the projection images are acquired, can be measured. An alternate, visual manner for the spatial resolution determination is provided by a line pair patterns embedded at 25mm depth of the 230mm*180mm*50mm (Length*Width*Height) block of BR12 material.

B.4.2. Complex background phantom

We have designed and manufactured a complex background phantom with which to perform reader studies using a full-field digital mammography system. The phantom is built using epoxy resin, which is breast tissue equivalent material simulating 70% glandular lobules in a 100% fat background. The formulation of each composition was optimized at energies between 15 keV and 40 keV. The ratio of glandular to fat is 50%. A set of four plates has been manufactured. In addition the researchers are working with the manufacturer to develop an optimal signal plate for the use with background

phantoms. Various signal plates have been considered and final design is now under construction.

B.5. MASTECTOMY SPECIMEN STUDY

The researchers have obtained tomosynthesis studies of mastectomy specimens in order to compare tomosynthesis and two-dimensional imaging for lesion detection. The data are acquired at 9 different projection angles using Rh-Rh target-filter combination and 25 to 28 kV depending on the thickness of the sample. The x-ray tube current is calculated to give a dose that is equivalent to the dose used to obtain a conventional mammogram of the same specimen. A new reconstruction algorithm allows axial (parallel to the image detector plate) tomosynthetic images, reconstructed as a 3D-volume through the whole specimen. While observing the data set on the computer it is possible to scan through the whole 3D-data set in a cine mode within few seconds while changing the window and level settings for the gray scale representation. The data set can be viewed using other slice orientations as well, i.e. coronal and sagittal orientations.

C. CONCLUSIONS

1) SNR for tomosynthesis is superior to conventional mammograms even with an equivalent radiation dose to that of a conventional mammogram.

2) MTF or spatial resolution for tomosynthesis is similar or slightly inferior to that of conventional mammography.

3) Complex phantom experiments indicate greatly improved lesion detection for both masses and calcifications using tomosynthesis as compared to conventional mammography.

4) A new reconstruction algorithm was developed that decreases the reconstruction time for tomosynthesis images and makes it possible to reconstruct any region of interest. This facilitates reconstructions of slices with very small intervals creating virtually a 3D data volume that can be looked at using different slice orientations; i.e. horizontal, coronal and sagittal.

Summary: The experiments and progress reported provides further evidence that tomosynthesis will be an important new tool in the diagnosis and characterization of breast cancer. The outcome of these experiments will be used to design the clinical tomosynthesis system and to determine the technical parameters that will be used for clinical imaging.

D. REFERENCES

Experimental and theoretical spectral optimization for digital mammography

Venkatakrishnan V, Yavuz M, Niklason LT, Opsahl-Ong B, Han S, Landberg C, Nevin R, Hamberg LM, Kopans DB

Proceedings of the SPIE International Conference on Medical Imaging 1999 Vol 3659, San Diego, CA, February 1999. Editors John M Boone and James T Dobbins

Digital Breast Imaging: Tomosynthesis and Digital Subtraction Mammography

Niklason LT, Kopans DB, Hamberg LM

Breast Disease 10(3,4) (1998) 1-14

Digital Tomosynthesis in Breast Imaging

Niklason LT, Christian BT, Niklason LT, Kopans DB, Castleberry, DE, Opsahl-Ong B, Landberg CE, Slanetez PJ, Giardino AA et al.,

Radiology 1997;205:399-406

E. SCIENTIFIC REPORTING OF THE WORK

Experimental and theoretical spectral optimization for digital mammography

Venkatakrishnan V, Yavuz M, Niklason LT, Opsahl-Ong B, Han S, Landberg C, Nevin R, Hamberg LM, Kopans DB

SPIE International Conference on Medical Imaging 1999, February 1999, San Diego, CA, Session: Physics of Medical Imaging

Antiscatter Grids: Are grids required for Digital Mammography? Niklason LT, Venkatakrishnan V, Opsahl-Ong B, Landberg C, Hamberg LM

84th Scientific Assembly and Annual meeting of the Radiological Society of North America, November 1998, Chicago, IL, Session: Physics: Mammography. Abstract, Radiology 1998, 209(P): 158.

Contrast-Detail Comparison of a Full-Field Digital Mammography System and a Screen-Film System. Rosol MS, Niklason LT, Venkatakrishnan V, Silvennoinen H, Kopans D, Hamberg LM Accepted for Presentation in 85th Scientific Assembly and Annual meeting of the Radiological Society of North America, November 1999, Chicago, IL

Antiscatter Grids: Are grids required for Digital Mammography? Niklason LT, Venkatakrishnan V, Opsahl-Ong B, Landberg C, Hamberg LM

Abstract, Radiology 1998, 209(P): 158.